An Ion-Pair Template for Rotaxane Formation and its Exploitation in an Orthogonal Interaction Anion-Switchahle Molecular Shuttle

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An Ion-Pair Template for Rotaxane Formation and its Exploitation in an Orthogonal Interaction Anion-Switchable Molecular Shuttle**

Michael J. Barrell,[1] David A. Leigh,[1,*] Paul J. Lusby[1,*] and Alexandra M. Z. Slawin[2]

[1]EaStCHEM, School of Chemistry, Joseph Black Building, University of Edinburgh, West Mains Road, Edinburgh, EH9 3JJ, UK.

[2]School of Chemistry, University of St. Andrews, Purdie Building, St. Andrews, Fife KY16 9ST, UK.

[*]Corresponding authors; P.J.L. e-mail: paul.lusby@ed.ac.uk, fax: (+44) 131-650-6453, website: http://www.catenane.net; D.A.L. e-mail: david.leigh@ed.ac.uk

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Supporting information:
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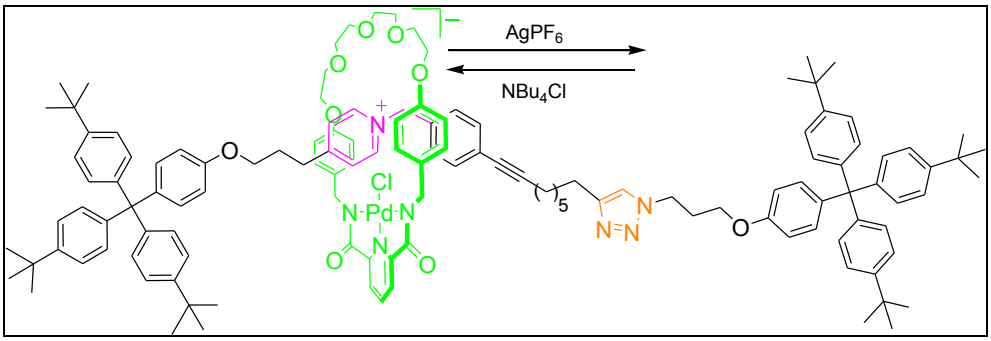
Graphical abstract:



Keywords:
Rotaxanes; molecular shuttles; template synthesis; palladium; anion recognition

Abstract

Chloride Control: The serendipitous discovery of a molecular recognition motif triggered by the formation of an anion-palladium coordination bond is exploited as both an efficient rotaxane-forming template and as the basis of a chloride-switchable molecular shuttle.

Main text

Despite significant advances[1] in anion-template methods for the construction of mechanically interlocked molecules,[2] the use of anions to induce changes in the relative positions of the components of catenanes and rotaxanes has proved particularly challenging,[3] especially in comparison to the widespread success achieved with other stimuli.[4-6] The few examples of anion-switchable molecular shuttles developed to date employ competition between the same types of weak interaction in both states of the molecule to achieve switching (solvation effects[3d,e] or the anion out-competing macrocycle hydrogen bonding acceptor groups for donor groups on the thread[3e,f]). Other features of anions, such as the propensity of halides to form strong coordination bonds to various transition metals, have yet to be exploited.[7] Here we report on the serendipitous discovery of a new efficient template for rotaxane formation and its use in the assembly of a chloride-switchable molecular shuttle which exhibits excellent positional integrity (>98%) of the ring in both states due to orthogonal modes of binding: direct intercomponent metal-ligand coordination in one state and a combination of tight ion-pairing, aromatic stacking interactions and CH···O and CH···Cl hydrogen bonding in the other.

The development of the new rotaxane-forming template was prompted by the chance observation that chloride displacement of the acetonitrile ligand of [(**L1**)Pd(CH_3CN)] using benzyl pyridinium chloride (**1**.Cl) was accompanied by encapsulation of the organic cation by the anionic PdCl-coordinated macrocycle [(**L1**)PdCl]$^-$ (Figure 1a).[8] The threaded nature of the complex {[(**L1**)PdCl].**1**} in $CDCl_3$ was clearly apparent from ^{1}H NMR spectroscopy (a distinct upfield shift in the pyridinium resonances with respect to those in **1**.Cl caused by shielding by the benzylic groups of the macrocycle, see Supporting Information) and was also found to persist in the solid state (Figure 1b and 1c) from X-ray crystallography of single crystals grown from a saturated CH_2Cl_2/EtOAc solution.[9]

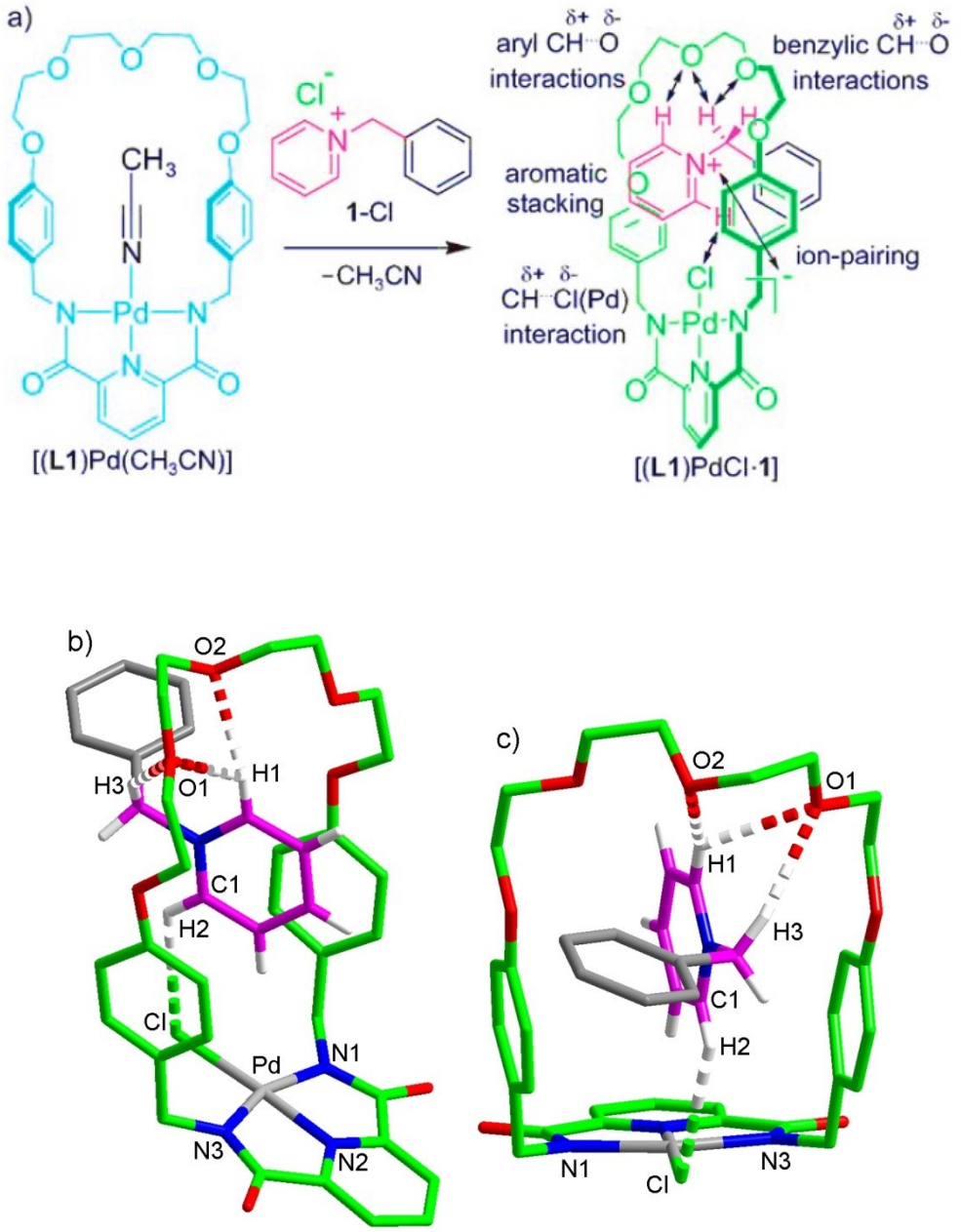


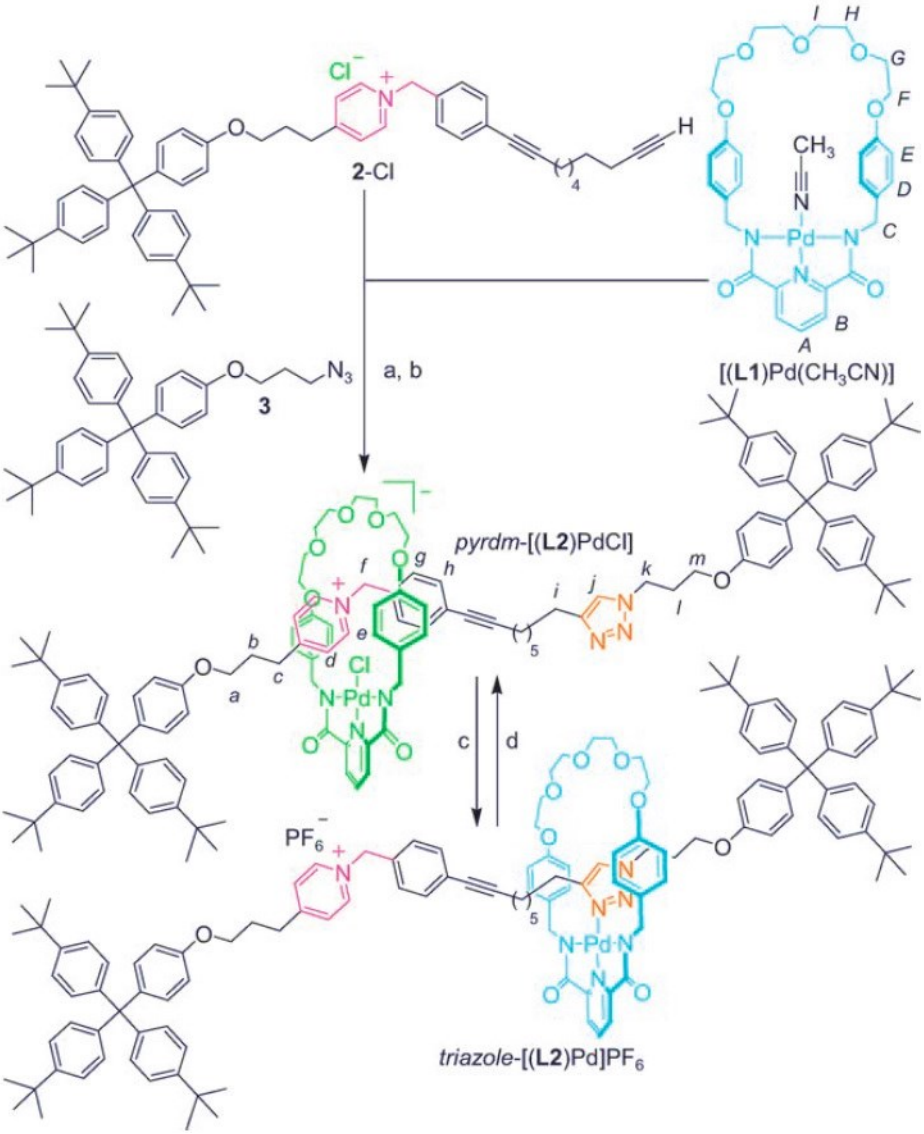
Figure 1. An allosteric anion-activated template for threading based on tight ion-pairing reinforced through multiple other non-covalent interactions. a) Synthesis of pseudorotaxane {[(**L1**)PdCl].**1**}. Conditions: CH_2Cl_2, 1 h, quantitative yield (employing **1**.PF_6 instead of **1**.Cl, or using DMSO instead of CH_2Cl_2, does not lead to pseudorotaxane formation). b) Side-on and c) face-on views of the X-ray crystal structure of {[(**L1**)PdCl].**1**}.[9] Nitrogen atoms are shown in blue, oxygen red, palladium silver, chlorine and the carbons of the macrocycle green, pyridinium purple, and other carbons gray. Selected bond lengths [Å] and angles [°]: N1-Pd 2.04, N2-Pd 1.93, N3-Pd 2.03, Cl-Pd 2.32, O1-*H3* 2.47, O2-*H1* 2.57, O2-*H1* 2.37, Pd-Cl 3.12, N1-Pd-N3 160.8, N2-Pd-Cl 176.4.

The solid state structure of {[(**L1**)PdCl].**1**} indicates that a broad range of noncovalent interactions are responsible for the assembly of the threaded architecture. In addition to the tight ion pair[10] (the pyridinium nitrogen atom is within 4 Å of atoms in the first coordination sphere of the formally negatively charged metal complex), aromatic stacking interactions between the aromatic rings of host and guest, aryl- and alkyl-CH···O hydrogen bonding between the polyether oxygen atoms and protons on carbons adjacent to the pyridinium nitrogen (C−O distances 3.19-3.36 Å), and CH···Cl(Pd) second coordination sphere interactions[7] (C−Cl distance 3.72 Å) all apparently contribute to the stability of the interpenetrated structure. Many of these primarily electrostatic interactions should be much weaker in more polar environments and, indeed, the ^{1}H NMR spectrum of {[(**L1**)PdCl].**1**} (see Supporting Information) shows the complex is largely unthreaded in [D_6]DMSO. The chloride anion is a vital component of the assembly process: [(**L1**)Pd(CH_3CN)] did not form a threaded complex when reacted with **1**.PF_6 in CH_2Cl_2, a result which suggested that the recognition motif could also be used as the basis of an anion-selective trigger.

A pyridinium chloride salt suitable for rotaxane synthesis (**2**.Cl) was prepared in four steps from 4-pyridinepropanol (see Supporting Information). Treatment of [(**L1**)Pd(CH_3CN)] with **2**.C1 in dichloromethane for 1 h, followed by reaction with **3** via a Cu(I)-catalyzed azide-alkyne 1,3-cycloaddition (CuAAC)[11] in the presence of *tris*-(benzyltriazolylmethyl)amine (TBTA)[12] and DIPEA (diisopropylethylamine) led to [(**L2**)PdCl] in 64% yield (Scheme 1). Mass spectrometry of this product was strongly suggestive of a rotaxane—the major peak, corresponding to [(**L2**)Pd]$^+$, does not fragment to the intact macrocycle and axle as would be expected for a non-interlocked salt—and the covalent capture of the threaded structure was confirmed when removal of palladium also did not cause separation of the components (see Supporting Information). Comparison of the ^{1}H NMR spectrum of [(**L2**)PdCl] (Figure 2b) with the chloride salt of the thread (Figure 2a), shows significant upfield shifts to the pyridinium resonances H_d, H_e and H_f, and adjacent protons (H_a and H_c). Other signals of the thread exhibit little change, indicating that the anionic PdCl-macrocycle is located overwhelmingly over the pyridinium station, i.e. the structure is *pyrdm*[13]-[(**L2**)PdCl] (Scheme 1).

The triazole group introduced by the CuAAC reaction can also act as a ligating station for the palladium-macrocycle.[14] Treatment of *pyrdm*-[(**L2**)PdCl] with $AgPF_6$ (1.1 equiv., Scheme 1 step c) smoothly precipitated AgCl giving quantitative conversion to a new rotaxane, [(**L2**)Pd]PF_6, in which the chloride ligand had been replaced by the non-coordinative PF_6 counter-ion. Comparison of the ^{1}H NMR spectrum of [(**L2**)Pd]PF_6 (Figure 2c) with that of the PF_6 salt of the thread (Figure 2d), shows that the signals of the pyridinium station (H_{d-f}) now occur at similar chemical shifts in thread and rotaxane, while the triazole resonance (Hj) and adjacent protons (e.g. H_i) are shifted upfield in the rotaxane indicating that removal of the chloride from the palladium center is accompanied by translocation of the palladium-macrocycle component to give *triazole*-[(**L2**)Pd]PF_6. Simple addition of tetrabutylammonium chloride to *triazole*-[(**L2**)Pd]PF_6 in

chloroform (Scheme 1, step d) reverses this process, producing a product with identical physical and spectroscopic properties to the original rotaxane, *pyrdm*-[(**L2**)PdCl].



Scheme 1. Synthesis and operation of chloride-switchable molecular shuttle $[(\mathbf{L2})Pd]^{+}$: a) CH_2Cl_2, 1 h; b) **3** (1.1 equiv), $Cu(CH_3CN)_4PF_6$ (0.2 equiv), TBTA (0.25 equiv), DIPEA (1 equiv), CH_2Cl_2/CH_3CN (7:1), 18 h, 64% (from **2**.Cl); c) $AgPF_6$ (1.1 equiv), acetone, 18 h, quantitative; d) Bu_4NCl (1.5 equiv), $CHCl_3$, quantitative.

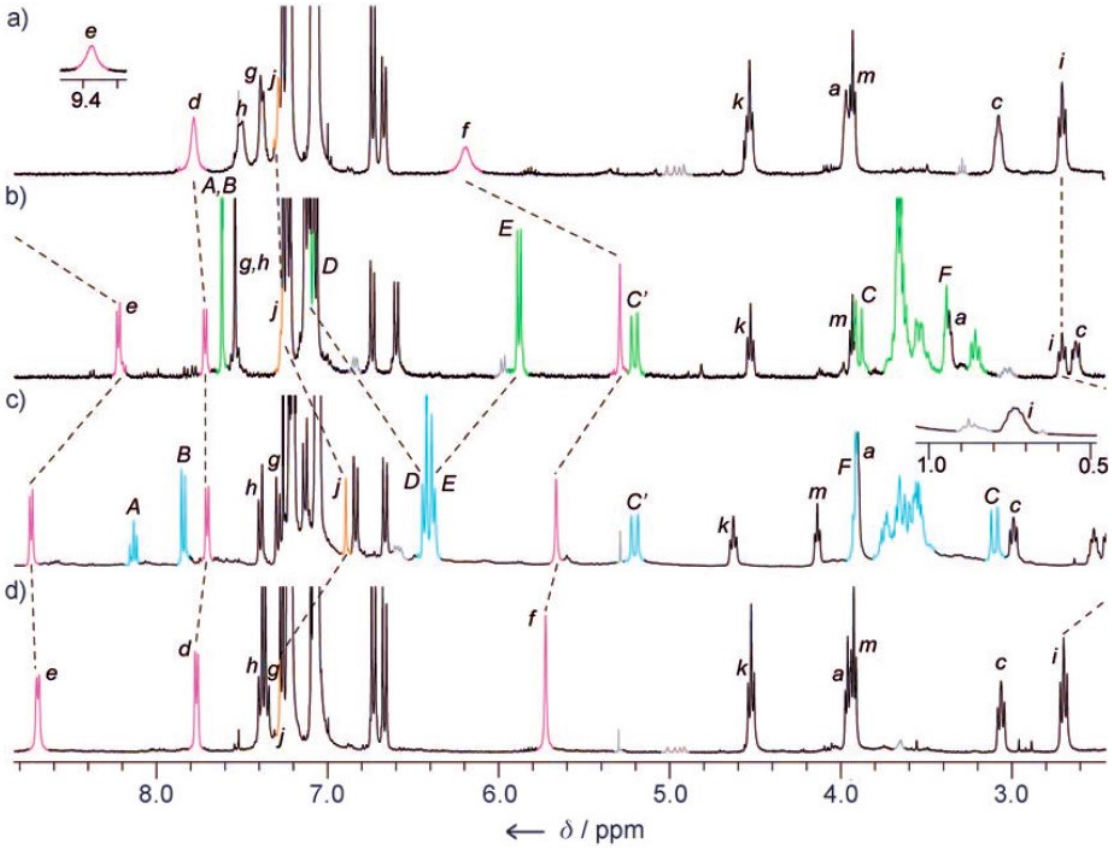


Figure 2. Partial ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) spectra of a) thread chloride salt, b) *pyrdm*-[(**L2**)PdCl], c) *triazole*-[(**L2**)Pd]PF_6,(d) thread PF_6 salt. The assignments correspond to the lettering shown in Scheme 1. Signals shown in gray are due to impurities and residual solvents.

The chance discovery of a molecular recognition motif that is triggered by the formation of an anion-palladium coordination bond has been exploited as both an efficient rotaxane-forming template and as the basis for a chloride-switchable molecular shuttle. The use of wholly different and orthogonal binding modes in the two states of the shuttle leads to exceptional positional integrity of the ring in both forms. Anion-activated allosteric templates could lead to new developments in sensors, logic gates, transport agents and molecular machines.

Experimental Section

Experimental procedure for the preparation of *pyrdm*-[(**L2**)PdCl]: **2**.Cl (59 mg, 0.066 mmol) and [(**L1**)Pd(CH_3CN)] (50 mg, 0.073 mmol) were stirred for 1 h in CH_2Cl_2 (7 mL) prior to the addition of **3** (43 mg, 0.073 mmol) and DIPEA (11 μL, 0.066 mmol). A solution of TBTA (9 mg, 0.017 mmol) and $Cu(CH_3CN)_4PF_6$ (6 mg, 0.0147 mmol) in CH_3CN (1 mL) was added and the reaction mixture allowed to stir

for a further 18 h. After this time the volatile compounds were removed under reduced pressure and the residue taken up in CH_2Cl_2 (10 mL). The resulting solution was washed with NH_4Cl (3 x 10 mL) and the aqueous phase re-extracted with CH_2Cl_2 (3 x 5 mL). The combined organic extracts were concentrated under reduced pressure and subjected to flash chromatography on silica gel (0-3% MeOH in CH_2Cl_2 as eluent) to give *pyrdm*-[(**L2**)PdCl] as a bright yellow solid (89 mg, 64%). For compound characterization, full synthetic details for all precursors and the switching experiments, see the Supporting Information.

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